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Current Aspects on Differentiating Relapses from Over-Infections in Symptomatic Inflammatory Bowel Diseases

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Dear Editor,

In their comparative retrospective cohort, Ahmad et al. [1] showed a higher rate of adverse events such as hospitalization, surgery, or delayed inflammatory bowel disease (IBD) treatment modification in patients with IBD tested positive with stool multiplex gastrointestinal pathogen panels (GPPs) for discrimination of diarrhea related to IBD exacerbation or infection, though positive predictive value of GPPs remained limited [1]. Gut microbiota of IBD patients includes a plethora of infectious species that could cause false positive results in GPP tests, thus delaying the decision of the appropriate treatment and reducing its clinical benefit [2]. Moreover, the interpretation of GPP test results in clinical practice is associated with some limitations, also mentioned by authors [1]. In this respect, several pathogens can occur not only asymptomatically (e.g., norovirus and Salmonella spp.) but also subclinically (e.g., Clostridium difficile non-toxigenic strains) in a colonization-like setting [3, 4], where connection with disease is uncertain. Additionally, an uncertainty exists regarding the cost-effectiveness of GPPs for suspected infectious gastroenteritis in hospital and community settings [5]. Interestingly, despite the well-described biases of GPPs in IBD [1] especially in terms of antimicrobial stewardship [6], all of the panels lack the capability to detect cytomegalovirus (CMV), which consists a substantial burden of IBD flares and steroids refractoriness being detected in 21–34% and 33–36% of these cases, respectively

[7]. Nevertheless, even if GPPs were able to detect fecal CMV-DNA, the sensitivity of polymerase chain reaction (PCR) for CMV-genome in stools seems to remain inferior to its detection in tissue samples depending also on the viral load [8]. Another important aspect that should be introduced is the role of confocal endomicroscopy (CE), which rises in IBD flare identification, as specific characteristics to define IBD activity have been suggested in many studies. Although still experimental, the assessment of the crypt morphology (number of colonic crypts, crypt tortuosity, crypt lumen), erosions, vascularity, cellular infiltrates within the lamina propria, number of goblet cells, gut barrier disruption, and leakage of fluorescein to the lumen could detect immediately and non-invasively the etiology of symptom exacerbation among IBD patients [9–11]. Furthermore, Clostridium difficile is visible and recognizable in vivo in the gut mucosa under CE, irrespective of symptoms manifestation [12], whereas other over-infections in patients with IBD have not been evaluated using CE, although it is known that these patients have intramucosal presence of bacteria more frequently than normal controls [9]. Nonetheless, this technique is still limited, lacking evidence-based data, expensive, and difficult to be performed to replace the conventional laboratory workup. Recently, by using the Luminex xTAG GPP, quantitative thresholds offer recognition of Clostridium difficile infection [13] which has been increasingly associated with IBD flares [14]. As deduced by the clinical necessity to differentiate IBD flares from over-infections beyond multiplex GPPs, further studies are required to develop and assess a novel, validated, and easy-to-perform, grading diagnostic index including clinical, laboratory, microbiological, and endoscopic findings to increase the sensitivity of a secure and accurate diagnosis in IBD symptomatic patients and obtain the potentiality of an immediate intervention.

Compliance with Ethical Standards

Conflict of interest: The authors declared that they have no conflict of interest.

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